CLAIMS

1. An amide derivative, which is a compound represented by the following general formula [1] in any of the following cases (A), (B) or (C), or a pharmaceutically acceptable salt thereof:

[Chemical 19]

R¹ represents any of groups of the following (1) through (3):

- (1) –CH₂-R¹¹ [R¹¹ represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group is substituted by a group selected from the group consisting of oxo, -CH₂-R¹¹¹ (R¹¹¹ represents a saturated, nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy and (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, and further, may be substituted by 1 or 2 same or different members selected from the group consisting of alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl],
- (2) -O-R¹² [R¹² represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group may be substituted by 1 to 3 same or different members selected from the group consisting of oxo, -CH₂-R¹²¹ (R¹²¹ represents a saturated,

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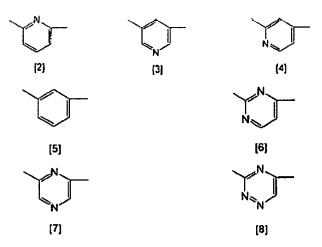
nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl], and

(3) -CH=R¹³ [R¹³ represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group may be substituted by 1 to 3 same or different members selected from the group consisting of oxo, -CH₂-R¹³¹ (R¹³¹ represents a saturated, nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl];

R² represents alkyl, halogen, haloalkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, acyl, amino, monoalkylamino, dialkylamino, nitro, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl or cyano;

R³ represents hydrogen, halogen or alkoxy;

Het1 represents any of groups of the following chemical formulas [2] to [8]: [Chemical 20]



Het2 represents pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl or 1,2-dihydropyridazinyl (the Het2 may be substituted by 1 to 3 same or different members selected from the group consisting of alkyl, halogen and amino);

wherein exception is made for a compound wherein R¹¹ is pyrrolidinyl, piperidinyl, piperazinyl or morpholinyl (each of the pyrrolidinyl, piperidinyl, piperazinyl and morpholinyl is substituted by a group selected from the group consisting of oxo, -CH₂-R¹¹¹ (R¹¹¹ represents a saturated, nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy and (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, and further, may be substituted by 1 or 2 same or different members selected from the group consisting of alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl); Het1 is a group of the formula [6]; and Het2 is pyrazinyl or pyridyl which may be substituted by alkyl;

(B)

R¹ represents -CH₂-R¹⁴ (R¹⁴ represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group may be substituted by 1 to 3 same or different members selected from the group consisting of alkyl, alkoxycarbonyl, halogen,

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haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl);

R² represents alkyl, halogen, haloalkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, acyl, amino, monoalkylamino, dialkylamino, nitro, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl or cyano;

R³ represents hydrogen, halogen or alkoxy;

Het1 represents any of groups of the following chemical formulas [9] and [10]: [Chemical 21]

Het2 represents pyridyl, pyrimidinyl, pyrazinyl, pyridazi98 nyl or 1,2-dihydropyridazinyl (the Het2 may be substituted by 1 to 3 same or different members selected from the group consisting of alkyl, halogen and amino);

(C)

R¹ represents any of groups of the following (1) through (3):

(1) –CH₂-R¹¹ [R¹¹ represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group is substituted by a group selected from the group consisting of oxo, -CH₂-R¹¹¹ (R¹¹¹ represents a saturated, nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy and (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, and further, may be substituted by 1 or 2 same or different members selected from the group consisting of alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl],

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- (2) –O-R¹² [R¹² represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group may be substituted by 1 to 3 same or different members selected from the group consisting of oxo, -CH₂-R¹²¹ (R¹²¹ represents a saturated, nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl], and
- (3) -CH=R¹³ [R¹³ represents a saturated, nitrogen-containing heterocyclic group. The saturated, nitrogen-containing heterocyclic group may be substituted by 1 to 3 same or different members selected from the group consisting of oxo, -CH₂-R¹³¹ (R¹³¹ represents a saturated, nitrogen-containing heterocyclic group), a saturated, nitrogen-containing heterocyclic group, aminoalkyl, monoalkylaminoalkyl, dialkylaminoalkyl, alkoxy, (5-methyl-2-oxo-1,3-dioxol-4-yl)methyl, alkyl, alkoxycarbonyl, halogen, haloalkyl, hydroxyalkyl, amino, monoalkylamino, dialkylamino, carbamoyl, monoalkylcarbamoyl and dialkylcarbamoyl];

R² represents alkyl, halogen, haloalkyl, hydroxyalkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, acyl, amino, monoalkylamino, dialkylamino, nitro, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl or cyano;

R³ represents hydrogen, halogen or alkoxy;

Het1 represents any of groups of the following chemical formulas [9] and [10]: [Chemical 22]

Het2 represents pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl or 1,2-dihydropyridazinyl (the Het2 may be substituted by 1 to 3 same or different members selected from the group consisting of alkyl, halogen and amino).

- 2. The amide derivative according to claim 1, which is a compound selected from the group consisting of the following compounds (1) to (14), or a pharmaceutically acceptable salt thereof:
- (1) 4-(1-methylpiperidin-4-ylidenemethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (2) 4-(1-methylpiperidin-4-yloxy)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (3) 4-(1-methylpiperazin-4-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[6-(3-pyridyl)pyrimidin-4-ylamino]phenyl}benzamide,
- (4) 4-(1-methylpiperazin-4-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[6-(5-pyrimidinyl)pyrimidin-4-ylamino]phenyl}benzamide,
- (5) (-)-4-((S)-3-maino-2-oxopyrrolidin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (6) 4-[(S)-2-(1-pyrrolidinylmethyl)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (7) 4-[3-(dimethylaminomethyl)azetidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (8) 4-[(S)-3-(1-pyrrolidinyl)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,

- (9) 4-{4-[(5-methyl-2-oxo-1,3-dioxol-4-yl)methyl]piperazin-1-ylmethyl}-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (10) 4-(4-methylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(4-pyridyl)thiazol-2-ylamino]phenyl} benzamide,
- (11) 4-[3-(dimethylamino)azetidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (12) 4-[(R)-3-(dimethylaminomethyl)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (13) 4-[(S)-3-(dimethylaminomethyl)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide, and
- (14) 4-[(3R,4R)-3-(dimethylamino)-4-methoxypyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide.
- 3. The amide derivative according to claim 1, which is a compound selected from the group consisting of the following compounds (1) to (37), or a pharmaceutically acceptable salt:
- (1) 3-difluoromethyl-4-(4-methylpiperazin-1-ylmethyl)-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (2) 3-ethyl-4-(4-methylpiperazin-1-ylmethyl)-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (3) 4-(1-methylpiperidin-4-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (4) 3,5-dichloro-4-[(S)-3-(dimethylamino)pyrrolidin-1-ylmethyl]-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,

- (5) 3-methoxy-4-(4-methylpiperazin-1-ylmethyl)-N-{3-[4-(5-bromopyridin-3-yl)pyrimidin-2-ylamino]-4-methylphenyl}benzamide,
- (6) 4-(4-ethylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (7) 4-(4-ethylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{3-[4-(5-bromopyridin-3-yl)pyrimidin-2-ylamino]-4-methylphenyl}benzamide,
- (8) 3-chloro-4-(4-methylpiperazin-1-ylmethyl)-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (9) 3-fluoromethyl-4-(1-methylpiperidin-4-ylmethyl)-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (10) 4-(4-methylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyridin-2-ylamino]phenyl}benzamide,
- (11) 4-(4-ethylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyridin-2-ylamino]phenyl}benzamide,
- (12) 4-(4-ethylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(3-pyridyl)pyridin-2-ylamino]phenyl} benzamide,
- (13) 4-(4-methylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(3-pyridyl)pyridin-2-ylamino]phenyl} benzamide,
- (14) 4-[4-(2-fluoroethyl)piperazin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (15) 4-[4-(2-hydroxyethyl)piperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,

- (16) 4-[(R)-3-(dimethylamino)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (17) 4-(1-piperazinylmethyl)-3-trifluoromethyl-N-{3-[4-(5-bromopyridin-3-yl)pyrimidin-2-ylamino]-4-methylphenyl} benzamide,
- (18) 4-(1-piperazinylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(3-pyridyl)pyridin-2-ylamino]phenyl} benzamide,
- (19) 4-(1-piperazinylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl} benzamide,
- (20) 4-(3-carbamoylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (21) 4-[(S)-3-(dimethylamino)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (22) 4-(3-carbamoyl-4-methylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (23) 4-((S)-3-methylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl} benzamide,
- (24) 4-((R)-3-methylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (25) 4-[(S)-3-(N,N-diethylamino)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (26) 4-[(2R,4S)-4-(dimethylamino)-2-methylpyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,

- (27) 4-((S)-3-aminopiperidinomethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (28) 4-[(S)-3-(dimethylamino)piperidinomethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (29) 4-((3S,4R)-3-amino-4-methylpyrrolidin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (30) 4-[(3S,4R)-3-(dimethylamino)-4-methylpyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (31) 4-[(S)-3-(methylamino)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (32) 4-((S)-3,4-dimethylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (33) 4-((R)-3,4-dimethylpiperazin-1-ylmethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (34) 4-[(3R,4R)-3-(dimethylamino)-4-methoxypyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(5-pyrimidinyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (35) 4-(1-methylpiperidin-4-yloxy)-3-trifluoromethyl-N-{4-methyl-3-[4-(3-pyridyl)pyrimidin-2-ylamino]phenyl}benzamide,
- (36) 4-(1-methylpiperidin-4-ylidenemethyl)-3-trifluoromethyl-N-{4-methyl-3-[4-(3-pyridyl)pyrimidin-2-ylamino]phenyl} benzamide, and
- (37) 4-[(R)-3-(dimethylaminomethyl)pyrrolidin-1-ylmethyl]-3-trifluoromethyl-N-{4-methyl-3-[4-(3-pyridyl)pyrimidin-2-ylamino]phenyl}benzamide.

- 4. A pharmaceutical composition comprising the amide derivative of any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof as an active ingredient.
- 5. A BCR-ABL tyrosine kinase inhibitor comprising the amide derivative of any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof as an active ingredient.
- 6. A therapeutic agent for chronic myelogenous leukemia comprising the amide derivative of any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof as an active ingredient.
- 7. A therapeutic agent for acute lymphoblastic leukemia comprising the amide derivative of any one of claims 1 to 3 or a pharmaceutically acceptable salt thereof as an active ingredient.
- 8. A therapeutic agent for acute myelogenous leukemia comprising the amide derivative of any one of claims 1 to 3 or a salt thereof as an active ingredient.